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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

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HINES, JANA A	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/650,261
Filing Date: August 27, 2003
Appellant(s): KIM, RAYMOND

Raymond Kim
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 3, 2008 appealing from the Office action mailed June 20, 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

4,806,312	GREENQUIST	2-1989
5,436,161	BERGSTROM et al.	7-1995

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-22 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Greenquist (US Patent 4,806,312; published February 21, 1989).

The claims are drawn to an apparatus comprising a molecular analyte layer and a film layer wherein:

(i) the molecular analyte layer comprises a molecular analyte immobilized on a molecular analyte solid support, wherein said molecular analyte comprises a molecular ligand binding site; and

(ii) the film layer comprises a molecular ligand zone having a molecular ligand, wherein, upon wetting of the molecular ligand zone, the molecular ligand can diffusibly migrate to the molecular ligand binding site of the molecular analyte to produce a detectable product.

Claim 15 is drawn to: (i) said molecular analyte comprises a first component of a donor-acceptor pair; (ii) said molecular ligand comprises a second component of said donor-acceptor pair; and (iii) said detectable product is a complex between the molecular ligand and the molecular analyte, wherein the position of the first component

of the donor- acceptor pair relative to the second component of the donor-acceptor pair allows detection of the complex. Claim 16 is drawn to the molecular analyte being a nucleic acid or a protein. Claim 17 is drawn to the molecular ligand being a nucleic acid or a protein. Claim 18 is drawn to: (i) said molecular analyte comprising an enzyme; (ii) the molecular ligand binding site having an active site of the enzyme; (iii) the molecular ligand comprising an enzyme substrate; and (iv) the detectable product is the enzyme substrate after being catalyzed by the enzyme.

Claim 19 is drawn to the molecular analyte being immobilized on said molecular analyte solid support by binding said molecular analyte to a capture agent immobilized on said molecular analyte solid support, wherein said binding is a molecular analyte specific binding event. Claim 20 is drawn to the capture agent being a protein or nucleic acid. Claim 21 is drawn to the film layer being a multilayered film layer, wherein said multilayered film layer comprises the molecular ligand zone and at least one additional zone, wherein said additional zone comprises a chemical or physical environment that is distinguishable from the molecular ligand zone. Claim 22 is drawn to the additional zone being below said molecular ligand zone and is porous or water soluble. Claim 25 is drawn to the film layer comprising at least two molecular ligands, wherein said at least two molecular ligands are distributed in an array format.

Greenquist teaches a multizone test device which provides a specific binding assay in a zoned or layered test strip or device (col. 5, lines 29-31). Greenquist teaches (i) the molecular analyte layer comprises a molecular analyte immobilized on a molecular analyte solid support (col. 5, lines 62-65), wherein said molecular analyte

comprises a molecular ligand binding site (col. 6, lines 26-19 and 37-40); and (ii) the film layer comprises a molecular ligand zone having a molecular ligand (col. 5, lines 57-61), wherein, upon wetting of the molecular ligand zone, the molecular ligand can diffusibly migrate to the molecular ligand binding site of the molecular analyte to produce a detectable product (col. 10, lines 12-20).

Greenquist teaches the labeled reagent being incorporated within the device, by being retained in the reagent zone and is free to migrate into the detection zone and capable of being bound to the immobilized interactive detection reagent in the detection zone (col. 5, lines 31-40). The reagent layer is incorporated with a reagent which comprises an immobilized form of the analyte (col. 5, lines 57-61). The labeled reagent is prebound to the separate reagent zone, since the binding is reversible upon the addition of liquid test medium to allow for diffusible migration (col. 10, lines 12-20). The device utilizes multiple reagent layers which are prepared using film formers (col. 17, lines 4-9); thereby teaching a unique film layer. The reagent layer is equivalent to the film layer since both the reagent layer and the film layer have an immobilized molecule. Greenquist teaches the detection layer being incorporated with an immobilized form of an interactive detection reagent (col. 5, lines 62-65). The detection layer is equivalent to the molecular analyte layer of the instant claims. Both the detection layer and the molecular analyte layer have an immobilized analyte on a solid support. The immobilizable material can be situated in any convenient location (col. 16, lines 54-65), thus Greenquist embraces an array format. The various layers of the multilayer device are self-supporting and positioned onto a support member (col. 12, lines 32-39).

Greenquist teaches the labeled reagent is a labeled form of a binding partner of the analyte and the immobilized reagent will be selected to be an immobilized form of the analyte (col. 5, lines 48-51). Therefore the labeled form of a binding partner of the analyte is equivalent to the molecular ligand found on the film layer (reagent layer) and the immobilized analyte detection reagent on the detection layer is equivalent to the molecular analyte immobilized on the molecular analyte layer. The analyte can be a peptide, protein nucleic acid or other molecule for which a specific binding partner or counterpart exist (col. 17, lines 30-36). It is noted, that the terms molecular analyte and molecular ligand are equivalent with the terms labeled reagent and detection reagent used by Greenquist, since both pairs refer to binding partners and their counterparts. Greenquist teaches the labeled reagent being permitted to diffuse and permeate into and through the reagent layer and into the detection layer and preferably provides only one available binding site for binding of the analyte to the labeled reagent (col. 6, lines 26-19 and 37-40).

Greenquist teaches the labeled reagent can comprise the analyte labeled with a chemical group having a detectable chemical or interactive property (col. 7, lines 13-15). The chemical group does not generate a detectable product or provide a detectable signal prior to interacting with an appropriate interactive detection reagent (col. 7, lines 17-19). Representative chemical groups include enzymatically active groups such as enzymes, enzyme substrates, specifically bindable ligands and energy transfer pairs (col. 8, lines 4-16). The energy transfer pairs are also known as donor-acceptor pairs, just as required by the claims. Greenquist teaches the label of the labeled reagent is an

enzyme substrate and the immobilized detection reagent is an enzyme capable upon interaction with the substrate of producing a detectable product (col. 8, lines 26-35). Greenquist teaches specific binding ligand labeled species such as biotin can be detected by adding an antibody to the hapten or protein (avidin) which binds the ligand tagged or labeled with a detectable molecule (col. 8, lines 20-25). Thereby acting as protein immobilized capture agents, just as required by the claims. Such detectable molecules produce measurable physical properties such as fluorescence or absorbance (col. 8, lines 25-26). Thus, the interaction between the labeled reagent and the interactive detection reagent provides a detectable signal or require interaction with an additional substance to provide a detectable signal (col. 8, lines 57-63).

The various layers of the multilayer device may comprise additional layers which are known to enhance or modulate the performance of the device (col. 14, lines 15-21). Greenquist teaches spreading layers, intermediate layers, timing layers and additional reagent or detection layers (col. 14, lines 21-59). The various layers may comprise a porous matrix wherein matrix materials include various porous fibrous materials or matrix forming materials of various layers of the multilayer device wherein such materials are made of agarose or the like (col. 15, lines 35-55). Therefore the zones are comprised of porous materials. Figures 4 and 5 show additional zones below the molecular ligand zone (detection zone) just as required by the claims.

Thus, Greenquist teaches the instantly claimed apparatus.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greenquist (US Patent 4,806,312; published February 21, 1989) as applied to claim 14 above, and further in view of Bergstrom et al., (US Patent 5,436,161; published July 25, 1995).

Claim 23 is drawn to the molecular ligand zone comprising a molecular ligand within a hydrogel. Claim 24 is drawn to the hydrogel comprising acrylamide or agarose.

Greenquist has been discussed above as teaching a multizone test device comprising: (i) the molecular analyte layer comprises a molecular analyte immobilized on a molecular analyte solid support (col. 5, lines 62-65), wherein said molecular analyte comprises a molecular ligand binding site (col. 6, lines 26-19 and 37-40); and (ii) the film layer comprises a molecular ligand zone having a molecular ligand (col. 5, lines 57-61), wherein, upon wetting of the molecular ligand zone, the molecular ligand can diffusibly migrate to the molecular ligand binding site of the molecular analyte to produce a detectable product (col. 10, lines 12-20). Greenquist teaches various layers of the multilayer device may comprise additional layers which are known to enhance or modulate the performance of the device (col. 14, lines 15-21). Greenquist teaches the various layers comprising a porous matrix wherein matrix materials include various

porous fibrous materials or matrix forming materials of various layers of the multilayer device wherein such materials are made of agarose or the like (col. 15, lines 35-55). However Greenquist does not teach the use of a hydrogel comprised of agarose.

Bergstrom et al., teach a hydrogel matrix coating sensing surfaces capable of selective biomolecular interaction to be used with biosensing devices (col. 1, lines 52-56). Biocompatible porous matrixes, like hydrogel bind to the film layer or solid support (col. 5, lines 49-52). Bergstrom et al., teach hydrogel coupling is essential for obtaining a sensing surface and is desirable for aiding protein compatibility and minimizing nonspecific interactions (col. 5, lines 52-55). Bergstrom et al., teach hydrogel is made from agarose or organic polymers such as poly-acrylamide materials (col. 5 lines 60-67).

Therefore it would have been prima facie obvious at the time of applicants' invention to apply a molecular ligand comprised within hydrogel comprising agarose as taught by Bergstrom et al., to the apparatus comprising a molecular analyte layer and a film layer as taught by Greenquist in order to obtain the essential coupling necessary for a sensing surface that enhances protein compatibility and minimizes nonspecific interactions. One of ordinary skill in the art would have a reasonable expectation of success by incorporating the well known alternative and functionally equivalent hydrogel material of Bergstrom et al., into the apparatus of Greenquist, since Greenquist already teach various porous fibrous layer materials made of agarose, wherein these multi-layers agarose formed materials are known to enhance the performance of the device; thereby yielding predictable results for one of skill in the art at the time of the invention.

Furthermore, no more than routine skill would have been required to exchange the commercially available and functionally equivalent hydrogel layer material of Bergstrom et al., into the apparatus of Greenquist since the art teaches hydrogel and other matrix forming materials are well known in the art for coating desired molecules onto a film layered solid surface in order to have a suitable apparatus with a biocompatible surface. Finally it would have been prima facie obvious to combine the invention of Greenquist and Bergstrom et al., to advantageously minimize undesired interactions by eliminating non-specific interactions between the surface and the proteins or biomolecules.

(10) Response to Argument

The rejection of claims 14-22 and 25 under 35 U.S.C. 102(b) as being anticipated by Greenquist (US Patent 4,806,312 published February 21,1989) is maintained for reasons already of record.

The rejection was on the grounds that Greenquist teaches an apparatus comprising a molecular analyte layer and a film layer wherein the molecular analyte layer comprises a molecular analyte immobilized on a molecular analyte solid support, wherein said molecular analyte comprises a molecular ligand binding site; and (ii) the film layer comprises a molecular ligand zone having a molecular ligand, wherein, upon wetting of the molecular ligand zone, the molecular ligand can diffusibly migrate to the molecular ligand binding site of the molecular analyte to produce a detectable product. Appellants' argue that Greenquist's labeled reagent is permitted to diffuse into the detection layer since only the labeled reagent/analyte complex is allowed to migrate.

In response to appellant's argument that Greenquist does not teach an analyte that is immobilized in one layer and layer and specifically binds a ligand to produce a detectable product, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use of specifically binding a ligand to produce a detectable product, then the teaching of Greenquist meets the claim. Furthermore, it is noted that appellants do not argue that the claimed invention results in a structural difference between the claimed invention and Greenquist, therefore appellants' arguments are not persuasive.

Appellants assert that the rejection is based on flawed reasoning and asserts that analytes and ligands are not equal binding partners. However it is noted that in appellants' clams 16 and 17; appellants list nucleic acid and protein as being the molecular analyte or the molecular ligand. Therefore, contrary to appellants' assertions, a biomolecule such as a protein or nucleic acid can in fact be capable of diffusing within a ligand zone or be immobilized to a fixed location. The analyte as Greenquist teach can be a peptide, protein nucleic acid or other molecule for which a specific binding partner or counterpart exist (col. 17, lines 30-36) such as a ligand. It is noted, that the terms molecular analyte and molecular ligand are interchangeable with the terms labeled reagent and detection reagent used by Greenquist, since both pairs refer to binding partners and their counterparts. Furthermore, it is the position of the Office that the labeled form of a binding partner of the analyte is equivalent to the molecular ligand

found on the film layer (reagent layer). Therefore appellants' argument is not persuasive.

Appellants' urge that the molecular ligand does not encompass the labeled reagent/analyte complex. However it is the examiner's position that the instant specification does not prevent the labeled reagent/analyte complex from being embraced by the definition of molecular ligand. The specification on page 4 states that "Molecular ligand" as used herein means any non-whole cell compound or molecule of interest for which a diagnostic test is desired. A molecular ligand can be, for example, a protein, peptide, carbohydrate, polysaccharide, glycoprotein, hormone, receptor, antigen, antibody, substrate, metabolite, transition state analog, cofactor, inhibitor, drug, dye, nutrient, growth factor, *etc*, without limitation. Thus, not only does the molecular analyte meet the definition, the labeled reagent/analyte complex is a non-whole cell complex and also a molecule of interest for which a diagnostic test is desired, hence the reason it is labeled and detected.

Finally, appellants are reminded that the claims are drawn to an apparatus where Greenquist teaches all the components of the apparatus including the molecular analyte layer comprises a molecular analyte immobilized on a molecular analyte solid support wherein said molecular analyte comprises a molecular ligand binding site; and the film layer comprises a molecular ligand zone having a molecular ligand wherein, upon wetting of the molecular ligand zone, the molecular ligand can diffusibly migrate to the molecular ligand binding site of the molecular analyte to produce a detectable product.

Therefore appellants' arguments are not persuasive because the teaching of Greenquist meets the limitations of appellants' claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The rejection of claims 23-24 under 35 U.S.C. 103(a) as being unpatentable over Greenquist in view of Bergstrom et al., is maintained for reasons already of record.

The rejection was on the grounds that no more than routine skill would have been required to modify the apparatus of Greenquist to incorporate hydrogel which is comprised of agarose as taught by Bergstrom et al., since the art already teaches that the layers of the apparatus may be of matrix forming agarose materials.

Appellants' assert that all of the elements of the claims have not been taught. Furthermore, in response to appellant's arguments against the Greenquist reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the rejection was over a combination of references, however the arguments only concentrate on the teaching of Greenquist.

Therefore, it is the examiner's position that Greenquist has been discussed above and only routine skill would have been required to incorporate hydrogel, since the art already teaches the advantages of hydrogel and matrix forming agarose materials. Thus appellants' arguments about the properties of the labeled reagent are misplaced, since the claims are drawn to an apparatus and not to the movements of the molecular ligand.

In response to appellant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, no more that routine skill would have been required in using a well known alternative and functionally equivalent material hydrogel when other matrix forming materials are known in the art to be essential for obtaining a sensing surface and is desirable for aiding protein compatibility and minimizing nonspecific interactions.

Appellants' urge that there is expectation of success. However it is the examiner's position that the expectation of some advantages is the strongest rationale for combining references. Moreover, the strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their

combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). See M.P.E.P 2144. However, contrary to appellants' assertions, one of ordinary skill in the art would have a reasonable expectation of success because no more than routine skill would have been required to use a known member of a class of materials such as hydrogel in a apparatus since other members of matrix forming materials comprised of agarose were known to be useful for the purpose of forming layers within the apparatus. Therefore appellants' arguments are not persuasive because the teaching of Greenquist in view of Bergstrom et al., meets the limitations of appellants' claims.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/JaNa Hines/

Conferees:

/Shanon A. Foley/

Supervisory Patent Examiner, Art Unit 1645

/Bruce Campell/

Supervisory Patent Examiner, Art Unit 1648